

Table 1 Formulation Examples 1-15

Table 1 (continued)

Constitution	Function	Components	Formulation Example 9	Formulation Example 10	Formulation Example 11	Formulation Example 12	Formulation Example 13	Formulation Example 14	Formulation Example 15
Nucleus	Nucleus Granule	ETHISPHERES	78.95	71.32	75.25	75.95	72.82	76.75	77.45
Drug-Carrying Layer	Drug Coating Agent Plasticizer	Beraprost sodium HPMC 2910 PEG 6000	0.12 3.62 0.73	0.12 3.79 0.75	0.12 3.68 0.74	0.12 3.62 0.73	0.12 3.79 0.75	0.12 3.68 0.74	0.12 3.62 0.73
	Subtotal		4.47	4.66	4.54	4.47	4.66	4.54	4.47
Sustained Release Layer 1	Skin Brittleness Agent	Glyceryl monoleate Glyceryl monopalmitate Glyceryl trimyristate Cetyl alcohol Stearic acid Talc	6.00 8.00 3.00 4.00	8.00 8.00 4.00 4.00	8.00 8.00 4.00 4.00	8.00 8.00 4.00 4.00	7.00 7.00 3.50 3.50	7.00 7.00 3.50 3.50	7.00 7.00 3.50 3.50
	Subtotal		9.00	12.00	12.00	12.00	10.50	10.50	10.50
Sustained Release Layer 2	Skin Brittleness Agent Plasticizer Dispersant	Eudragit NE30D Cellulose acetate Ethyl cellulose Talc Triethyl citrate Polysorbate 80	6.00 6.00 1.20 0.36 0.02	6.00 6.00 1.30 0.39 0.02	6.00 6.00 1.20 0.36 0.02	6.00 6.00 1.20 0.36 0.02	6.50 6.00 1.30 0.39 0.02	6.50 6.00 1.30 0.39 0.02	6.00 6.00 1.20 0.36 0.02
	Subtotal		7.58	12.02	8.21	7.58	12.02	8.21	7.58
Other	Lubricant	Talc	0.50	0.50	0.50	0.50	0.50	0.50	0.50
	Total		100.50	100.50	100.50	100.50	100.50	100.50	100.50

Unit: mg/capsule

Table 2 Formulation Examples 16-18

Constitution	Function	Components	Formulation Example 16	Formulation Example 17	Formulation Example 18
Nucleus	Nucleus Granule	SUGLETS	71.70	69.84	68.78
	Drug	Beraprost Sodium	0.12	0.12	0.12
Drug-Carrying Layer	Coating Agent	Poloxamer 188	3.79	3.68	3.62
	Plasticizer	PEG 4000	0.75	0.74	0.73
	Subtotal		4.66	4.54	4.47
Barrier	Coating Agent	HPMC 603	2.31	2.24	2.19
	Brittleness Agent	Talc	0.46	0.45	0.44
	Subtotal		2.77	2.69	2.63
Sustained Release Skin Layer 1	Coating Agent	Glyceryl Palmitooleate	8.08	7.93	7.71
	Brittleness Agent	Talc	4.04	3.965	3.855
	Subtotal		12.12	11.90	11.57
Sustained Release Skin Layer 2	Coating Agent	Eudragit RS30D	6.22	7.89	8.93
	Brittleness Agent	Talc	1.24	1.58	1.79
	Plasticizer	Myvacet 945	1.26	1.55	1.81
	Dispersant	Polysorbate 80	0.02	0.02	0.03
	Subtotal		8.74	11.04	12.56
Other	Lubricant	Talc	0.50	0.50	0.50
	Total		100.50	100.50	100.50

Unit: mg/capsule

Table 3 Comparative Examples 1 and 2

Constitution	Function	Components	Formulation Example 16	Formulation Example 17
Nucleus	Nucleus Granule	NONPAREIL	97.27	89.86
Drug-Carrying Layer	Drug	Beraprost Sodium	0.12	0.12
	Coating Agent	HPMC 2910	2.37	2.37
	Plasticizer	PEG 6000	0.24	0.24
Subtotal		100.00	2.73	
Sustained Release Skin Layer	Coating Agent	Eudragit RS-100	3.97	
	Plasticizer	Eudragit RS-100L		1.32
	Brittleness Agent	triethyl citrate Talc	0.53	1.59
Subtotal			7.41	
Other	Lubricant	Talc	0.50	0.50
Total		100.50	100.50	

Unit: mg/capsule

Table 4 Human PK Parameters of Comparative Examples 1 and 2 and Formulation Example 16

Examples	C <sub>max</sub> (pg/mL)	T <sub>max</sub> (hr)	AUC (hr·pg/mL)	Relative Availability (%)
Comparative Example 1	414±201	0.4±0.1	449±131	100±29
Comparative Example 2	21± 9	2.8±1.1	128± 82	29±18
Formulation Example 16	84±26	2.8±0.8	319±119	71±27

mean±S.D. (n=5-12)

Relative Availability: Relative percentage taken the AUC of the immediate release preparation of Comparative Example 1 as 100%

Figure 1

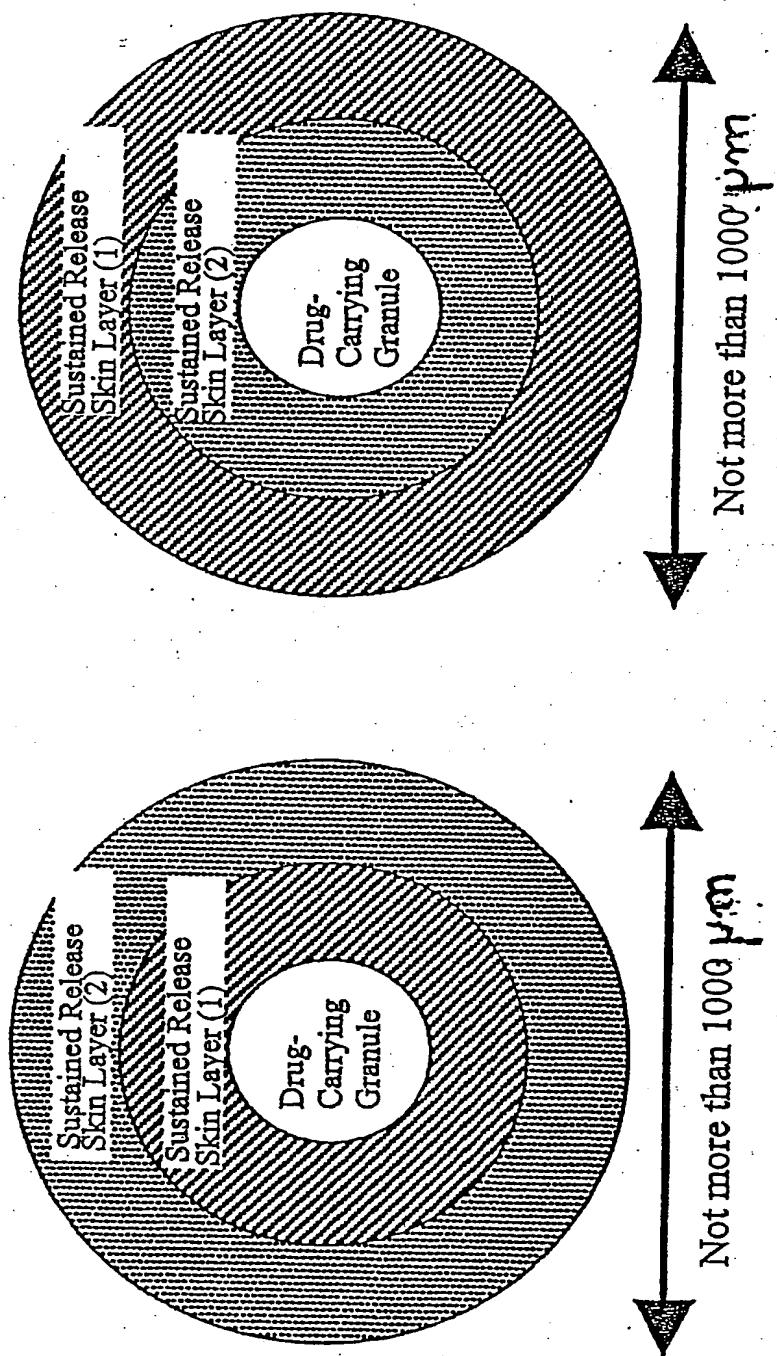


Figure 2

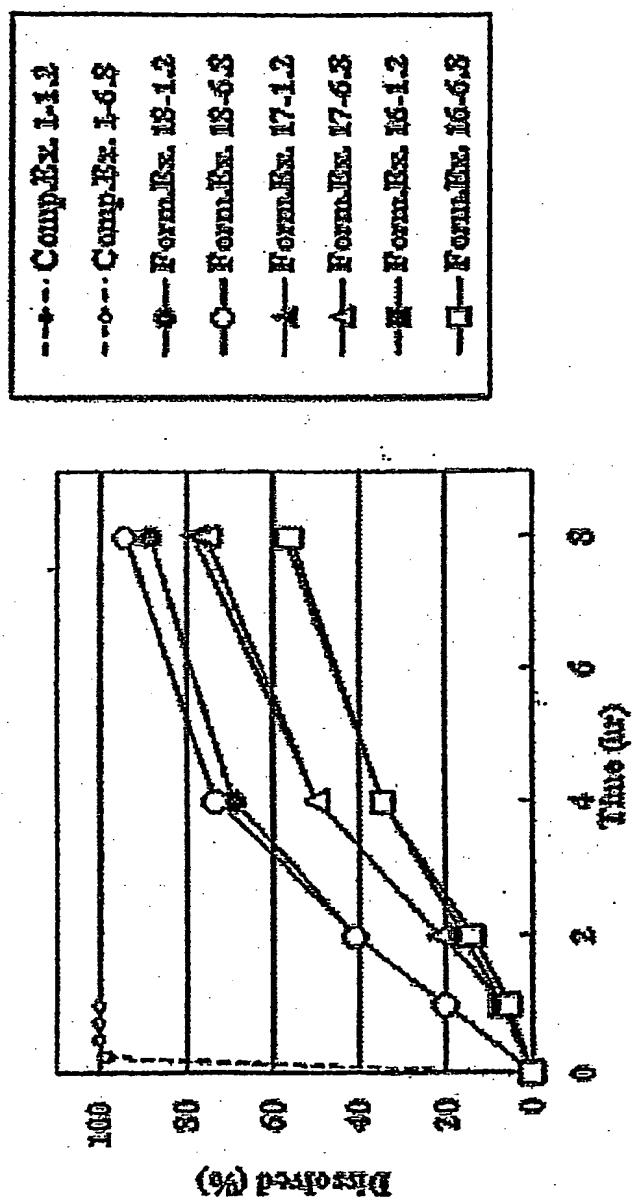


Figure 3

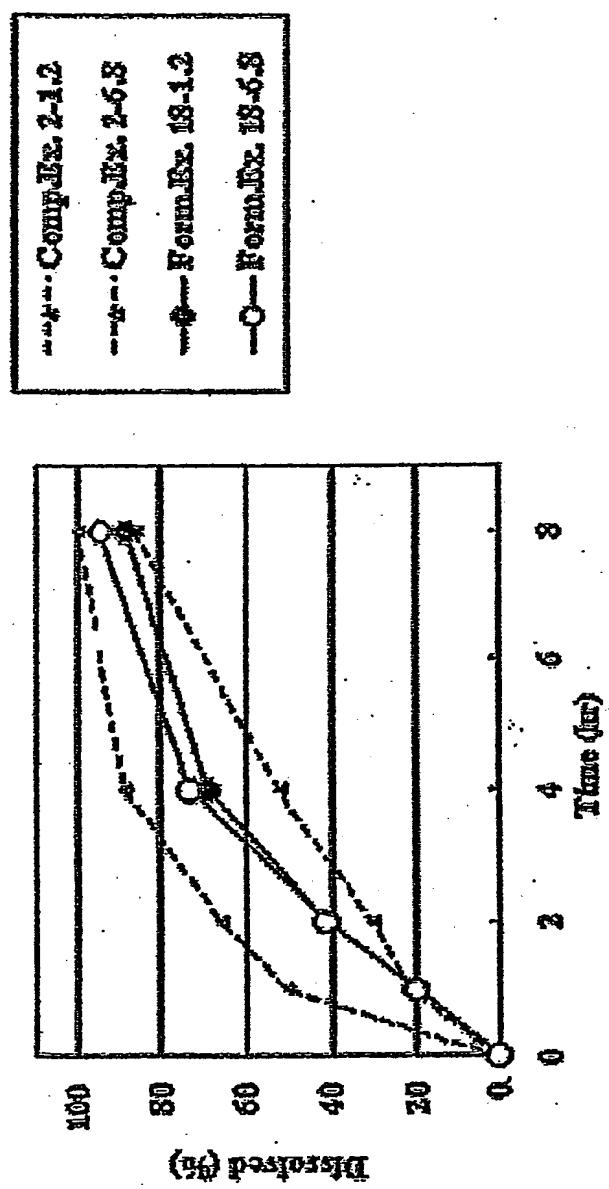


Figure 4

